Non Technical Abstract

Current cancer gene therapy strategies have been hindered by the ability to acheive efficient and specific gene delivery to cancer cells. To this end, the Gene Therapy Program at UAB has developed a major focus in the area of vector improvement. Specifically, we have demonstrated that adenoviral vectors can be modified to accomplish dramatically enhanced gene transfer to human tumor cells. It is our hypothesis that modifications of adenoviral vectors that increase tumor cell transduction will enhance the therapeutic effect in the context of ovarian cancer gene therapy. Accordingly, this research proposal includes a human gene therapy protocol for ovarian and extraovarian cancer patients with persistent or recurrent disease. This Phase I protocol will 1)determine the maximally tolerated dose and spectrum of toxicities encountered with intraperitoneal delivery of an antibody fragment (Fab') modified, fibroblast growth factor (FGF2) enhanced adenovirus encoding Herpes Simplex Virus thymidine kinase (HSV-TK) given in combination with intravenous ganciclovir (GCV) in previously treated ovarian and extraovarian patients, 2)determine the safety of administration of intraperitoneally delivered FGF2-Fab' modified adenovirus encoding HSV-TK given in combination with intravenous GCV in previously treated ovarian/extraovarian cancer patients, 3)determine gene transfer efficiency of intraperitoneally administered FGF2-Fab' modified recombinant adenovirus, and 4)determine the ability of intraperitoneally delivered FGF2-Fab' modified adenovirus encoding HSV-TK to modify the host immune response. This novel vector strategy has been highly promising in preclinical studies. It is anticipated that the studies thus described would establish the safety and provide an indication of the efficacy of this approach in human subjects with ovarian cancer.